# Computer vision AI to characterize human health and disease

### James Zou Stanford University Chan-Zuckerberg Investigator

(video removed)



### What do you see?

69 years old man

Left face sagging

White silver hair

Bytes of information

**Deep wrinkles** 

**Elongated face** 

Gordon J et al. NEJM 2012

### What do you see?



MBs of information

Gordon J et al. NEJM 2012

### Information is visual



Heart ultrasound

(video removed)

Tumor biopsy



Microglia

(video removed)

How would you describe these?

Goal: comp. vision  $\rightarrow$  new language of morphology and biology/disease

### **Computer vision advances**

(video removed)



Ghorbani, Wexler, Zou, Kim NeurIPS 2019

### Vision for heart

(video removed)





Video AI for assessing cardiac function. *Nature* 2020. Ouyang, He, Ghorbani, Yuan, Ebinger, Langlotz, Heidenreich, Harrington, Liang, Ashley, Zou



### Vision for heart

Heart disease is the leading cause of death in the US. 1in 4 death (>600k/year)



Echocardiogram is routinely used to assess heart function. >10 million/year in the US. Each one costs >\$1000.



### Human vision is the driver of cardiac assessment

Heart disease is the leading cause of death in the US. 1in 4 death (>600k/year)

(video removed)

Human vision is expensive, time-consuming and variable.



### Computer vision can be faster and more reliable

Algorithm output

(video removed)

EchoNet assessed chamber area



# Algorithm mimics clinical workflow

#### **EchoNet-Dynamic**



Liver

•••

Idea: use temporal segmentation to focus attention of model.

### Achieves expert performance in new hospital



Examples

(video removed)

# Algorithm robust to noisy videos

Maintains good performance when 50% of video is corrupted



# Open dataset and code

EchoNet-Dynamic

A Large New Cardiac Motion Video Data Resource for Medical Machine

Learning

Home Introduction Motivation Dataset Baseline Model Leaderboard Accessing Dataset Citation

90 -	×.	÷.		E.		Dataset Label Variables								Collaborators are only visible to	
> <sup>eo -</sup>						/ariable	Descrip	tion						folder owner and	a co-owners.
30 -					I	FileName	Hashed	Hashed file name used to link videos, labels, and annotations					BA Owner		
					I	EF	Ejection	Ejection fraction calculated from ESV and EDV					Do David Ouya	ang	
·					- I	ESV	End sys	End systolic volume calculated by method of discs					Contrast Area		
90 - 80 -					I	EDVEnd diastolic volume calculated by method of discsHeightVideo HeightWidthVideo Width							A System Account Co-owner		
					I								System Account	ount	
					I								Co-owner		
30 -					I	$\operatorname{FPS}$	Frames	Frames Per Second						Johanna Ki	m
0 -				1	NumFrames	Numbe	Number of Frames in whole video								
Ó 3Ó	eo so	o so eo X	90 Ó	sio eio si	• 5	Split	Classifi	cation of the	rain/valida	tion/test s	sets used fo	or benchma	arking	Externally S	Shared
0X1B0895E4993C 1F79	0X1B1798BF5669 FB07	0X1B2089E659E6 AA87	0X1B2241C91CC DEF05	0X1B2900BF089A D45F	0X1B6045BB5315 1A4A	0X1B7833C5A54B 5FF2	0X1B48047F9A40 121	0X1B165975B5EF 65D9	0X1B170168A644 9950	0X1B53202748E0 AB3F	0X1B37993135742 8C0	0X1BA7A8147245 AB28	OX1BA8C753E08F B53F	0X1BA53DA5F128 AB92	0X1BA265AD5BF 096E5
0X1BA556585D2F E6A7	0X1BACE554294D DF8	0X1BB19B668CF2 A22E	0X1BB609E66AC3 4DE	0X1BB47462D0C4 70D5	0X1BB91877C1F2 F21E	0X1BC515434037 562D	0X1BCA569AEE7F CFC6	0X1BCA2217072B CB55	0X1BCAECCA681 C2F1A	OX1BCC6B1BA8F EBC5	0X1BCC98038783 10C8	0X1BCD0AD72EC B908A	0X1BD5EEAC641 B0443	0X1BD7A625C9D A5292	OX1BD453F455D3 ODEA
OXTBE3FBED90CB	0X1BE64129E54E4	0X1BEA6959BDF3	OXTBED31FBCDA	0X1BF00F2E669B	0X1BF56B66ECD9	0X1BFF8D71CA00	0X1C0BDFA4E539	0X1C1A328EA29B	0X1C1E4272FA76	DX1C1F4EA2045C	OXIC4BA7E6CC2	0X1C5B6810C622	0X1C5E88A03170	0X1C7A7B6A9AF	0X1C7C2D50F32

Largest public dataset of medical videos.

# Vision for histopathology

Histology image (breast cancer)



#### **Clinician annotation**



- Tumour
- Normal

# Single cell analysis loses spatial information



# ST-Net: histology to spatial genomics

#### ST-Net generated expression



Normal

Accurately generates spatial expression of >100 genes.

# ST-Net: histology to spatial genomics

ST-Net generated expression



Normal

Accurately generates spatial expression of >100 genes.

**Experimental** 

# Works well across patients

Histology image

ST-Net generated FASN expression Experimental FASN measurement







#### Clinician annotation



Paper: He, Bergenstrahle, Stenbeck, Abid, Andersson, Borg, Maaskola, Lundeberg, Zou. Nature Biomedical Eng. (2020)

# Spatial transcriptomics technology

Spatial transcriptomics measurements of hundreds of genes in breast tumor



#### Each probe is ~100 microns

#### Bryan He



#### Joakim Lundeberg



# ST-Net: image to transcriptome profile translation



ST-Net accurately imputes >100 genes at 100 micron resolution. Trained on over >30k spatially resolved transcriptomes.

# Validated on external patient samples

AUC on test 2



AUC on test set 1

Each dot = one gene.

100 genes that we can generate accurate spatial profile:

- tumor makers
- immune markers
- mobility and architecture genes

### ST-Net maps sub-cellular morphology to expression





Input image



### Expression — morphology association

#### Association betw expression of each gene to morphology

	Nucleus size $(pixels^2)$	Axis Ratio	Nuclear Density
GNAS	$0.21~(p = 5 \times 10^{-4})$	-0.25 $(p = 6 \times 10^{-6})$	$0.26~(p=3 imes 10^{-3})$
ACTG1	$0.25~(p=5 imes 10^{-4})$	-0.23 ( $p = 5 \times 10^{-4}$ )	$0.14~(p = 2 \times 10^{-1})$
FASN	$0.25 \ (p = 5 \times 10^{-4})$	-0.23 ( $p = 6 \times 10^{-6}$ )	$0.00~(p = 4 \times 10^{-2})$
DDX5	$0.27~(p = 7 \times 10^{-5})$	-0.25 ( $p = 6 \times 10^{-6}$ )	$0.23~(p = 1 \times 10^{-2})$
XBP1	$0.18 \ (p = 5 \times 10^{-4})$	-0.17 ( $p = 5 \times 10^{-4}$ )	0.12 $(p = 1 \times 10^{-2})$

#### + 100 other genes



# Works well on previously collected images

Any histology image Computationally synthesized FASN expression T-Net Computationally synthesized FASN expression

Can apply to archival images, e.g. from clinical labs.

Quantifies tumor heterogeneity and immune infiltration

# **Applications**



Insta-pathology: real-time generation of spatial genomics profiles.

Prognosis + treatment design using tumor heterogeneity.

Cell biology: linking genes to cellular morphology

#### Resources

Papers and codes available www.james-zou.com

Video-based AI for cardiac assessment.

Ouyang et al. Nature 2020

Deep learning for generating spatial transcriptomics. He et al. *Nature Biomedical Engineering* 2020





Thanks to J. Lundeberg, E. Ashley and support from Chan-Zuckerberg initiative.